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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,939	01/02/2004	Edward G. Niles	11520.0333	2269

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EXAMINER	
LE, EMILY M	
ART UNIT	**PAPER NUMBER**
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/750,939	NILES ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2004 and 10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *13-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☒ Claim(s) *8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, SEQ ID NO: 14 in the reply filed on 10/10/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Claims

2. Claims 1-29 are pending. Claims 13-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/10/2006. Claims 1-12 are under examination.

Claim Objections

3. Claim 8 is objected to because of the following informalities: The recitation "CH3, CH3O, NH2 and CH3CH2NH2" should be "CH_3, CH_3O, NH_2 and $CH_3CH_2NH_2$". Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4, 7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Gryaznov et al.[1]

The claims are directed to an oligonucleotide that is between 8 to about 40 nucleotides in length, and comprising an oligoribonucleotide portion having the sequence of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence UUUUUNU, wherein N can be A, G, U or C, and a flanking region at the 5' end, the 3' end or both ends of the oligoribonucleotide portion comprising at least one ribonucleotide, deoxyribonucleotide, modified ribonucleotide, or modified deoxyribonucleotide. Claim 2, which depends on independent claim 1, requires the oligonucleotide to be between 9 and 36 nucleotides long, which is limited to between 9 and 22 nucleotides by claim 3, which depends on claim 2; which is further limited to between 9 and 13 nucleotides by claim 4, which depends on claim 3. Claim 7, which depends on claim 1, requires at least one of the nucleotide present in the oligonucleotide to have a modified sugar, at the 2'O position. Claim 9, which depends on claim 1, requires the flanking region to have an internucleotide linkage selected from the group consisting of phosphorothiols, methylphosphonates and phosphoramidites. Claim 10 is directed at a composition comprising the oligonucleotide of claim 1.

Gryaznov et al. teaches SEQ ID NO: 1. [Columns 21-22] SEQ ID NO: 1 of Gryaznov et al. has the sequence: UUUUUUUUUT. SEQ ID NO: 1 of Gryaznov et al. is 10 nucleotides in length, have the sequence: UUUUUNU, wherein N is U; and have a flanking region at the 5' and 3' ends of the oligoribonucleotide portion comprising at

[1] Gryaznov et al., U.S. Patent No. 5684143, published 11/04/1997.

least one ribonucleotide, deoxyribonucleotide and modified deoxyribonucleotide. Gryaznov et al. also teaches the modification of least one of the nucleotide present in SEQ ID NO: 1. In the instant case, Gryaznov et al. teaches the modification of the sugar, specifically the 2'O position. Additionally, Gryaznov et al. also teaches the use of phosphoramidites as the internucleotide linkage in the flanking region. [Example 6 and Table 1, column 18.]

In the instant case, SEQ ID NO: 1 of Gryaznov et al. is the same as those instantly claimed. Hence, Gryaznov et al. also teaches a composition comprising the nucleotide. Therefore, Gryaznov et al. anticipates the claimed invention.

It is noted that the claims contain a whereby clause, wherein the clause sets forth that the claimed oligonucleotide to be capable of causing premature termination of transcription of poxvirus genes. This whereby clause has been considered. However, it is found that the whereby clause, which suggests or makes optional but does not require steps to be performed and does not limit a claim to a particular structure, do not limit the scope of a claim or claim limitation. See MPEP § 2106 (II)(C). Thus, the claimed invention remains to be an oligonucleotide that is between 8 to about 40 nucleotides in length, and comprising an oligoribonucleotide portion having the sequence of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence UUUUUNU, wherein N can be A, G, U or C, and a flanking region at the 5' end, the 3' end or both ends of the oligoribonucleotide portion comprising at least one ribonucleotide, deoxyribonucleotide, modified ribonucleotide, or modified deoxyribonucleotide.

As noted above, SEQ ID NO: 1 of Gryaznov et al. is the same as those instantly claimed. Therefore, Gryaznov et al. anticipates the claimed invention.

6. Claims 1-6 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Deng et al.[2]

The claims are directed to an oligonucleotide that is between 8 to about 40 nucleotides in length, and comprising an oligoribonucleotide portion having the sequence of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence UUUUUNU, wherein N can be A, G, U or C, and a flanking region at the 5' end, the 3' end or both ends of the oligoribonucleotide portion comprising at least one ribonucleotide, deoxyribonucleotide, modified ribonucleotide, or modified deoxyribonucleotide. Claim 2, which depends on independent claim 1, requires the oligonucleotide to be between 9 and 36 nucleotides long, which is limited to between 9 and 22 nucleotides by claim 3, which depends on claim 2; which is further limited to between 9 and 13 nucleotides by claim 4, which depends on claim 3. Claim 5, which depends on claim 1, limits the oligonucleotide to a Markush group of sequences, wherein one member includes SEQ ID NO. 14. Claim 6, which depends on claim 1, limits the oligonucleotide to SEQ ID NO: 14. Claim 10 is directed at a composition comprising the oligonucleotide of claim 1. Claim 11, which depends on claim 10, limits the oligonucleotide to SEQ ID NO: 14.

Deng et al. teaches an oligonucleotide having the sequence of UUUUUUUUU. The sequence of Deng et al. has the sequence UUUUUNU, wherein N is U, and a flanking region at the 5' end, the 3' end or both ends of the oligoribonucleotide portion

comprising at least one ribonucleotide. This sequence of Deng et al. is the same as the claimed SEQ ID NO: 14, which has 9 nucleotides in length. Deng et al. also teaches a composition comprising the oligonucleotide. [Paragraph bridging left and right columns, page 19559.] In the instant case, Deng et al. teaches the claimed oligonucleotide and a composition comprising said oligonucleotide. Hence, Deng et al. anticipates the claimed invention.

It is noted that the claims contain a whereby clause, wherein the clause sets forth that the claimed oligonucleotide to be capable of causing premature termination of transcription of poxvirus genes. This whereby clause has been considered. However, it is found that the whereby clause, which suggests or makes optional but does not require steps to be performed and does not limit a claim to a particular structure, do not limit the scope of a claim or claim limitation. See MPEP § 2106 (II)(C). Thus, the claimed invention remains to be an oligonucleotide that is between 8 to about 40 nucleotides in length, and comprising an oligoribonucleotide portion having the sequence of SEQ ID NO: 1. SEQ ID NO: 1 has the following sequence UUUUUNU, wherein N can be A, G, U or C, and a flanking region at the 5' end, the 3' end or both ends of the oligoribonucleotide portion comprising at least one ribonucleotide, deoxyribonucleotide, modified ribonucleotide, or modified deoxyribonucleotide.

As noted above, SEQ ID NO: 1 of Gryaznov et al. is the same as those instantly claimed. Therefore, Gryaznov et al. anticipates the claimed invention.

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[2] Deng et al. Factor-dependent release of Nascent RNA by ternary complexes of vaccinia RNA polymerase. The Journal of Biological Chemistry. August 09, 1996, Vol. 271, No. 32, 19556-19562.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gryaznov et al., as applied to claims 1 and 7, in view of Eckstein et al.[3]

Claim 8, which depends on claim 7, which depends on claim 1, requires the modification at the 2'O position of the sugar group be selected from the group consisting of CH_3, CH_3O, NH_2 and $CH_3CH_2NH_2$.

The significance of Gryaznov et al., as it applies to claims 1 and 7, is provided above. In the instant case, as noted above, while Gryaznov et al. does teach a modification at the 2'O position of the sugar group, however, the modification made by Gryaznov et al. is not selected from the group consisting of CH_3, CH_3O, NH_2 and $CH_3CH_2NH_2$.

However, the deficiency noted of Gryaznov et al. is cured by the teachings of Eckstein et al. Eckstein et al. teaches the modification made at the 2'O position of the sugar group either a halogen or an amino (NH_2). [Lines 28-40, column 3; Figures 1B and 4.] At the cited passage, Eckstein et al. teaches that the preferred the modification made at the 2'O position of the sugar group to be either a halogen or an amino (NH_2). Eckstein et al. teaches that the incorporation of such modification significantly increases

RNA stability against enzymatic cleavage. In the instant case, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made to have modify the 2'O position of the sugar group with an amino. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to increase RNA stability against enzymatic cleavage. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Eckstein et al. recognizes the modification of the 2'O position of the sugar group with a halogen or an amino as functional equivalents of one another.

9. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gryaznov et al., as applied to claim 10.

Claim 12, which depends on claim 10, requires the composition comprising the oligonucleotide to comprise a pharmaceutically acceptable carrier.

The significance of Gryaznov et al., as it applies to claim 10, is provided above. In the instant case, it is not readily apparent if the composition of Gryaznov et al. comprises a pharmaceutically acceptable carrier. However, it should be noted that Gryaznov et al. does envision the addition of a pharmaceutically acceptable carrier to his composition. [Lines 41-42, column 9.] At the cited passage, Gryaznov et al. envisioned the composition with a pharmaceutically acceptable carrier. Hence, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to include a pharmaceutically acceptable carrier. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so

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[3] Eckstein et al. U.S. Patent No. 5672695, published 09/30/1997.

to regulate drug concentration, solubility, chemical stabilization, viscosity, absorption enhancement, pH or the like of the composition. [Lines 40-46, column 9.] One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the addition of pharmaceutically acceptable carrier to a composition is routinely practiced in the art.

10. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deng et al., as applied to claim 1, in view of Eckstein et al.

Claim 7, which depends on claim 1, requires at least one of the nucleotide present in the oligonucleotide to have a modified sugar, at the 2'O position. Claim 8, which depends on claim 7, requires the modification at the 2'O position of the sugar group be selected from the group consisting of CH_3, CH_3O, NH_2 and $CH_3CH_2NH_2$.

The significance of Deng et al., as it applies to claim 1, is provided above. In the instant case, Deng et al. does not teach the modification at the 2'O position of the sugar group.

However, the deficiency noted of Deng et al. is cured by the teachings of Eckstein et al. Eckstein et al. teaches the modification made at the 2'O position of the sugar group either a halogen or an amino (NH_2). [Lines 28-40, column 3; Figures 1B and 4.] At the cited passage, Eckstein et al. teaches that the preferred the modification made at the 2'O position of the sugar group to be either a halogen or an amino (NH_2). Eckstein et al. teaches that the incorporation of such modification significantly increases RNA stability against enzymatic cleavage. In the instant case, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made to

have modify the 2'O position of the sugar group with an amino (NH_2) or a halogen. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to increase RNA stability against enzymatic cleavage. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Eckstein et al. recognizes the modification of the 2'O position of the sugar group significantly increases RNA stability against enzymatic cleavage.

11. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deng et al., as applied to claim 1, in view of Eckstein et al.

Claim 9, which depends on claim 1, requires the flanking region to have an internucleotide linkage selected from the group consisting of phosphorothiols, methylphosphonates and phosphoramidites.

The significance of Deng et al., as it applies to claim 1, is provided above. In the instant case, the sequence of Deng et al. does not have flanking region that has an internucleotide linkage selected from the group consisting of phosphorothiols, methylphosphonates and phosphoramidites.

However, the deficiency noted of Deng et al. is cured by the teachings of Eckstein et al. Eckstein et al. teaches the use of modified internucleotidic linkages, in combination with a modification at the 2'O position of the sugar group, to provide increase stability against degradation. [Lines 20-35, column 5.] The modification that Eckstein et al. teaches includes internucleotide linkage selected from the group consisting of phosphorothiols and methylphosphonates. Thus, it would have been

prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to have modified the internucleotidic linkages to phosphorothiols and methylphosphonates. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to increase stability against degradation, when combined with a 2'O modification. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Eckstein et al. teaches the increase in stability against degradation with such modification.

12. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deng et al., as applied to claim 10, in view of Gryaznov et al.

Claim 12, which depends on claim 10, requires the composition comprising the oligonucleotide to comprise a pharmaceutically acceptable carrier.

The significance of Deng et al., as it applies to claim 10, is provided above. In the instant case, it is not readily apparent if the composition of Deng et al. comprises a pharmaceutically acceptable carrier.

However, the deficiency noted of Deng et al. is cured by the teachings of Gryaznov et al. Gryaznov et al. teaches the addition of a pharmaceutically acceptable carrier with oligonucleotides to regulate the concentration, solubility, chemical stabilization, viscosity, absorption enhancement, pH or the like of the composition. [Lines 40-46, column 9.] Hence, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to include a pharmaceutically acceptable carrier. One of ordinary skill in the art, at the time the

invention was made, would have been motivated to do so to regulate drug concentration, solubility, chemical stabilization, viscosity, absorption enhancement, pH or the like of the composition. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the addition of pharmaceutically acceptable carrier to a composition is routinely practiced in the art.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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